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FILE 'CAPLUS' ENTERED AT 14:17:27 ON 21 MAY 2003

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COST IN U.S. DOLLARS

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ENTRY	SESSION

FULL ESTIMATED COST

2.80 3.01

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=> s kit#(10a) Fv (10a) (oligonucleotide# or nucleic acid#)

L1 0 KIT#(10A) FV (10A) (OLIGONUCLEOTIDE# OR NUCLEIC ACID#)

=> s Fv (p) (coupl### or attach### or bind###) (p) (oligonucleotide# or nucleic acid#)

L2 111 FV (P) (COUPL### OR ATTACH### OR BIND###) (P) (OLIGONUCLEOTIDE# OR NUCLEIC ACID#)

=> s l2 and kit#

L3 4 L2 AND KIT#

=> d l3 1-4 bib ab

L3 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS

AN 2002:575193 CAPLUS

DN 137:139362

TI Human antibodies and fragments derived from phage display library for selective cancer therapy and diagnosis

IN Hagai, Yocheved; Lazarovits, Janette; Guy, Rachel; Lipschitz, Orly; Szanton, Esther; Levanon, Avigdor; Plaksin, Daniel; Peretz, Tuvia

PA Bio-Technology General Corp., USA

SO PCT Int. Appl., 232 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

PATENT NO.

KIND DATE

APPLICATION NO. DATE

PI WO 2002059264 A2 20020801 WO 2001-US49440 20011231
 WO 2002059264 A3 20030306
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
 UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
 TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
 CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-751181 A1 20001229
 AB The present invention is directed to a peptide or polypeptide comprising
 an Fv mol., a construct thereof, a fragment of either, or a
 construct of a fragment having enhanced **binding** characteristics
 so as to **bind** selectively and/or specifically to a target cell
 in favor of other cells, wherein the **binding** selectivity or
 specificity is primarily detd. by a first hypervariable region, and
 wherein the Fv is a scFv or a dsFv, and optionally having one or
 more tags. The enhanced **binding** is directed to a substantially
 exposed and/or over-expressed **binding** site on or in a target
 comprising a cell in favor of other cells on or in which the
binding site is not substantially available and/or expressed. The
 invention is further directed to a method for isolating such peptides and
 polypeptides from a phage display library and to the **nucleic**
acid mols. encoding them. The invention provides for a
 pharmaceutical compn. comprising the peptide or polypeptide and
kits for diagnosis and treatment of disease, specifically cancer,
 most specifically acute myeloid leukemia.

L3 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
 AN 2002:540186 CAPLUS
 DN 137:92741
 TI Oligonucleotide-attached monoclonal antibodies or fragments for
 immunodetection of epitopes on molecules and molecule interactions via
 fluorescent dyes
 IN Greene, Mark I.; Zhang, Hong Tao; Li, Bin; Liu, Qindu; Murali, Ramchandran
 PA USA
 SO U.S. Pat. Appl. Publ., 11 pp., Cont.-in-part of U.S. Ser. No. 783,896.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002094534	A1	20020718	US 2001-977716	20011015
	US 2002028450	A1	20020307	US 2001-783896	20010215
	WO 2002066980	A1	20020829	WO 2002-US3640	20020208
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 2000-624946	A2	20000725		
	US 2001-783896	A2	20010215		
	US 2001-977716	A	20011015		
AB	Methods, systems and kits are provided for detecting mols. expressing a selected epitope in a sample through use of an epitope				

detector contg. a single chain Fv for the selected epitope or a constrained epitope specific CDR, CDR mimetic or engineered CDR structure attached to an oligonucleotide. The method is useful for identifying a CDR, CDR mimetic or engineered CDR structure for use in an epitope detector or a ligand, a pharmaceutical drug or therapeutic agent.

L3 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS
 AN 2002:172436 CAPLUS
 DN 136:229055
 TI Immuno-arna fluorescent detection of epitopes
 IN Greene, Mark I.; Zhang, Hongtao
 PA USA
 SO U.S. Pat. Appl. Publ., 9 pp., Cont.-in-part of U. S. Ser. No. 624,946.
 CODEN: USXXCO

DT Patent
 LA English
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002028450	A1	20020307	US 2001-783896	20010215
	US 2002094534	A1	20020718	US 2001-977716	20011015
	WO 2002066980	A1	20020829	WO 2002-US3640	20020208
	W:	AB, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
PRAI	US 2000-624946	A2	20000725		
	US 2001-783896	A2	20010215		
	US 2001-977716	A	20011015		

AB The authors disclose methods for detecting mols. expressing a selected epitope in a sample through use of a single chain Fv for the selected epitope, or a constrained epitope-specific CDR, attached to an dsDNA oligonucleotide. The dsDNA oligonucleotide contains the promoter for the T7 polymerase. In one example, an immobilized p185neu receptor was detected using epitope-specific scFv-oligonucleotide conjugate and fluorescent measurement of amplified RNA.

L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS
 AN 2002:90343 CAPLUS
 DN 136:133596
 TI Sensitive detection of epitopes using antibody-based nucleic acid amplification
 IN Greene, Mark I.; Eberwine, James H.; Kacharina, Janet Estee; Zhang, Hong Tao
 PA The Trustees of the University of Pennsylvania, USA
 SO PCT Int. Appl., 25 pp.
 CODEN: PIXXD2

DT Patent
 LA English
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002008757	A1	20020131	WO 2001-US22645	20010718
	W:	AB, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,			

RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
 VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 EP 1305625 A1 20030502 EP 2001-953537 20010718
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 PRAI US 2000-624946 A 20000725
 WO 2001-US22645 W 20010718
 AB The authors disclose methods and reagents for detecting mols. expressing a
 selected epitope in a sample through use of a "universal epitope
 detector". In one embodiment, the universal epitope detector is an
 anti-histidine tag single chain **Fv attached** to an T7
 promoter-contg. double-stranded **oligonucleotide**. In an
 illustrative example, HER2 is captured to a solid phase using an
 immobilized antibody and the analyte sandwiched with a second His-tagged
 antibody. Addn. of the universal epitope detector and amplification of
 synthesized radiolabeled RNA provides for a sensitive readout and
 quantitation of HER2.
 RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>

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=> s complementarity determining region#(P) (coupl### or attach### or bind###) (10a) (oligonucleotide# or nucleic acid#)
L1 39 COMPLEMENTARITY DETERMINING REGION#(P) (COUPL### OR ATTACH### OR BIND###) (10A) (OLIGONUCLEOTIDE# OR NUCLEIC ACID#)

=> s l1 and polymerase#
L2 3 L1 AND POLYMERASE#

=> s l2 and kit#
L3 0 L2 AND KIT#

=> d l2 1-3 bib ab kwic

L2 ANSWER 1 OF 3 MEDLINE
AN 2001250834 MEDLINE
DN 21244632 PubMed ID: 11320219
TI Protein quantification from complex protein mixtures using a proteomics methodology with single-cell resolution.
AU Zhang H T; Kacharina J E; Miyashiro K; Greene M I; Eberwine J
CS Department of Pathology, Abramson Institute for Cancer Research, University of Pennsylvania, Philadelphia, PA 19104-6082, USA.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2001 May 8) 98 (10) 5497-502.

Journal code: 7505876. ISSN: 0027-8424.

CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 200106
 ED Entered STN: 20010618
 Last Updated on STN: 20030105
 Entered Medline: 20010614

AB We have developed an extremely sensitive technique, termed immuno-detection amplified by T7 RNA polymerase (IDAT) that is capable of monitoring proteins, lipids, and metabolites and their modifications at the single-cell level. A double-stranded oligonucleotide containing the T7 promoter is conjugated to an antibody (Ab), and then T7 RNA polymerase is used to amplify RNA from the double-stranded oligonucleotides coupled to the Ab in the Ab-antigen complex. By using this technique, we are able to detect the p185(her2/neu) receptor from the crude lysate of T6-17 cells at 10(-13) dilution, which is 10(9)-fold more sensitive than the conventional ELISA method. Single-chain Fv fragments or complementarity determining region peptides of the Ab also can be substituted for the Ab in IDAT. In a modified protocol, the oligonucleotide has been coupled to an Ab against a common epitope to create a universal detector species. With the linear amplification ability of T7 RNA polymerase, IDAT represents a significant improvement over immuno-PCR in terms of sensitivity and has the potential to provide a robotic platform for proteomics.

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L2 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 AN 2001:301838 BIOSIS
 DN PREV200100301838
 TI Protein quantification from complex protein mixtures using a proteomics methodology with single-cell resolution.
 AU Zhang, Hong-Tao; Kacharmina, Janet E.; Miyashiro, Kevin; Greene, Mark I. (1); Eberwine, James
 CS (1) Departments of Pathology and Laboratory Medicine, Abramson Institute for Cancer Research, University of Pennsylvania, Philadelphia, PA, 19104-6082; greene@reo.med.upenn.edu, eberwine@mscf.med.upenn.edu USA
 SO Proceedings of the National Academy of Sciences of the United States of America, (May 8, 2001) Vol. 98, No. 10, pp. 5497-5502. print.
 ISSN: 0027-8424.

DT Article
 LA English
 SL English
 AB We have developed an extremely sensitive technique, termed immuno-detection amplified by T7 RNA polymerase (IDAT) that is

capable of monitoring proteins, lipids, and metabolites and their modifications at the single-cell level. A double-stranded oligonucleotide containing the T7 promoter is conjugated to an antibody (Ab), and then T7 RNA polymerase is used to amplify RNA from the double-stranded oligonucleotides coupled to the Ab in the Ab-antigen complex. By using this technique, we are able to detect the p185her2/neu receptor from the crude lysate of T6-17 cells at 10-13 dilution, which is 109-fold more sensitive than the conventional ELISA method. Single-chain Fv fragments or complementarity determining region peptides of the Ab also can be substituted for the Ab in IDAT. In a modified protocol, the oligonucleotide has been coupled to an Ab against a common epitope to create a universal detector species. With the linear amplification ability of T7 RNA polymerase, IDAT represents a significant improvement over immuno-PCR in terms of sensitivity and has the potential to provide a robotic platform for proteomics.

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IT . . .
 Systems of Organisms
 cell; pyramidal neuron: nervous system
 IT Diseases
 cancer: neoplastic disease
 IT Chemicals & Biochemicals
 RNA; T7 RNA polymerase; antibody; double-stranded
 oligonucleotide: T7 promoter; p185-her2/neu receptor; peptide
 IT Alternate Indexing
 Neoplasms (MeSH)
 IT Methods & Equipment
 ELISA: analytical method; Western blot: analytical method;
 immuno-detection amplified by T7 RNA polymerase: analytical
 method

L2 ANSWER 3 OF 3 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

AN 2001177003 EMBASE

TI Protein quantification from complex protein mixtures using a proteomics methodology with single-cell resolution.

AU Zhang H.-T.; Kacharmina J.E.; Miyashiro K.; Greene M.I.; Eberwine J.

CS M.I. Greene, Department of Pathology, Abramson Inst. for Cancer Research, University of Pennsylvania, Philadelphia, PA 19104-6082, United States. greene@reo.med.upenn.edu

SO Proceedings of the National Academy of Sciences of the United States of America, (8 May 2001) 98/10 (5497-5502).

Refs: 36

ISSN: 0027-8424 CODEN: PNASA6

CY United States

DT Journal; Article

FS 029 Clinical Biochemistry

LA English
 SL English
 AB We have developed an extremely sensitive technique, termed immuno-detection amplified by T7 RNA **polymerase** (IDAT) that is capable of monitoring proteins, lipids, and metabolites and their modifications at the single-cell level. A double-stranded oligonucleotide containing the T7 promoter is conjugated to an antibody (Ab), and then T7 RNA **polymerase** is used to amplify RNA from the double-stranded **oligonucleotides coupled** to the Ab in the Ab-antigen complex. By using this technique, we are able to detect the p185(her/neu) receptor from the crude lysate of T6-17 cells at 10(-13) dilution, which is 10(9)-fold more sensitive than the conventional ELISA method. Single-chain Fv fragments or **complementarity determining region** peptides of the Ab also can be substituted for the Ab in IDAT. In a modified protocol, the **oligonucleotide** has been **coupled** to an Ab against a common epitope to create a universal detector species. With the linear amplification ability of T7 RNA **polymerase**, IDAT represents a significant improvement over immuno-PCR in terms of sensitivity and has the potential to provide a robotic platform for proteomics.

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CT Medical Descriptors:
 *protein determination
 analytic method
 lipid analysis
 promoter region
 conjugation
 antigen antibody complex
 cell lysate
 enzyme linked immunosorbent assay
 human
 nonhuman
 rat
 controlled study
 human cell
 animal cell
 article
 priority journal
 *proteome
 RNA **polymerase**
 oligonucleotide
 antibody
 epitope

RN (RNA **polymerase**) 9014-24-8

PROCESSING COMPLETED FOR L2
L4 1 DUP REM L2 (2 DUPLICATES REMOVED)

=> d l4 bib ab kwic

L4 ANSWER 1 OF 1 MEDLINE DUPLICATE 1
AN 2001250834 MEDLINE
DN 21244632 PubMed ID: 11320219
TI Protein quantification from complex protein mixtures using a proteomics methodology with single-cell resolution.
AU Zhang H T; Kacharmina J E; Miyashiro K; Greene M I; Eberwine J
CS Department of Pathology, Abramson Institute for Cancer Research, University of Pennsylvania, Philadelphia, PA 19104-6082, USA.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2001 May 8) 98 (10) 5497-502.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200106
ED Entered STN: 20010618
Last Updated on STN: 20030105
Entered Medline: 20010614
AB We have developed an extremely sensitive technique, termed immuno-detection amplified by T7 RNA polymerase (IDAT) that is capable of monitoring proteins, lipids, and metabolites and their modifications at the single-cell level. A double-stranded oligonucleotide containing the T7 promoter is conjugated to an antibody (Ab), and then T7 RNA polymerase is used to amplify RNA from the double-stranded oligonucleotides coupled to the Ab in the Ab-antigen complex. By using this technique, we are able to detect the p185(her2/neu) receptor from the crude lysate of T6-17 cells at 10(-13) dilution, which is 10(9)-fold more sensitive than the conventional ELISA method. Single-chain Fv fragments or complementarity determining region peptides of the Ab also can be substituted for the Ab in IDAT. In a modified protocol, the oligonucleotide has been coupled to an Ab against a common epitope to create a universal detector species. With the linear amplification ability of T7 RNA polymerase, IDAT represents a significant improvement over immuno-PCR in terms of sensitivity and has the potential to provide a robotic platform for proteomics.
AB We have developed an extremely sensitive technique, termed immuno-detection amplified by T7 RNA polymerase (IDAT) that is capable of monitoring proteins, lipids, and metabolites and their modifications at the single-cell level. A double-stranded oligonucleotide containing the T7 promoter is conjugated to an antibody (Ab), and then T7 RNA polymerase is used to amplify RNA from the double-stranded oligonucleotides coupled to the Ab in the Ab-antigen complex. By using this technique, we are able to detect the p185(her2/neu) receptor from . . . of T6-17 cells at 10(-13) dilution, which is 10(9)-fold more sensitive than the conventional ELISA method. Single-chain Fv fragments or complementarity determining region peptides of the Ab also can be substituted for the Ab in IDAT. In a modified protocol, the oligonucleotide has been coupled to an Ab against a common epitope to create a universal detector species. With the linear amplification ability of T7 RNA polymerase, IDAT represents a significant improvement over immuno-PCR in terms of sensitivity and has the potential to provide a robotic platform. . .

=> dup rem l1
PROCESSING COMPLETED FOR L1

=> d 15 1-15 bib ab

L5 ANSWER 1 OF 15 MEDLINE DUPLICATE 1
AN 2003009407 MEDLINE
DN 22403668 PubMed ID: 12515537
TI Mutational analysis of a sequence-specific ssDNA binding lupus
autoantibody.
AU Cleary Joanne; Glick Gary D
CS Department of Chemistry, University of Michigan, Ann Arbor, Michigan
48109-1055, USA.
NC GM 46831 (NIGMS)
SO BIOCHEMISTRY, (2003 Jan 14) 42 (1) 30-41.
Journal code: 0370623. ISSN: 0006-2960.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200302
ED Entered STN: 20030108
Last Updated on STN: 20030302
Entered Medline: 20030228

AB 11F8 is a murine anti-ssDNA monoclonal autoantibody isolated from a lupus
prone autoimmune mouse. This mAb binds sequence specifically, and prior
studies have defined the thermodynamic and kinetic basis for
sequence-specific recognition of ssDNA (Ackroyd, P. C., et al. (2001)
Biochemistry 40, 2911-2922; Beckingham, J. A. and Glick, G. D. (2001)
Bioorg. Med. Chem. 9, 2243-2252). Here we present experiments designed
to identify the residues on 11F8 that mediate sequence-specific,
noncognate, and nonspecific recognition of ssDNA and their contribution to
the overall binding thermodynamics. Site-directed mutagenesis of an 11F8
single-chain construct reveals that six residues within the
complementarity determining regions of 11F8
account for ca. 80% of the binding free energy and that there is little
cooperativity between these residues. Germline-encoded aromatic and
hydrophobic side chains provides the basis for nonspecific recognition of
single-stranded thymine nucleobases. Sequence-specific recognition is
controlled by a tyrosine in the heavy chain along with a somatically
mutated arginine residue. Our data show that the manner in which 11F8
achieves sequence-specific recognition more closely resembles RNA-
binding proteins such as U1A than other types of **nucleic
acid binding proteins**. In addition, comparing the
primary sequence of 11F8 with clonally related antibodies that differ by
less than five amino acids suggests that somatic mutations which confer
sequence specificity may be a feature that distinguishes glomerulotrophic
pathogenic anti-DNA from those that are benign.

L5 ANSWER 2 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2002:344020 BIOSIS
DN PREV200200344020
TI The regulation of autoimmune anti-DNA response by idiotype-specific
cytotoxic T-cells in BALB/c mice.
AU Lim, So-Yon (1); Ghosh, Swapan K. (1)
CS (1) Life Sciences, Indiana State University, 6th and Chestnut, Terre
Haute, IN, 47809 USA
SO FASEB Journal, (March 20, 2002) Vol. 16, No. 4, pp. A687.
<http://www.fasebj.org/>. print.
Meeting Info.: Annual Meeting of the Professional Research Scientists on
Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
ISSN: 0892-6638.
DT Conference
LA English
AB CD8+ cytotoxic T-cell (CTL) mediated control of autoreactive B-cells was

investigated using a monoclonal antibody (mAb), 2C3 (IgG1, k), derived from phthalate-immunized BALB/c mice. Since the idiotype (Ids) of 2C3 share a striking homology with those of an anti-DNA mAb, BV04-01 (IgG2b, k), from autoimmune prone (NZBxW) F1 mice, we compared its **binding specificity** for phthalate with that for autologous DNA and **oligonucleotides**. The results show that 2C3 Ig has a strong affinity both for phthalate and DNA and, in particular, for the oligonucleotides, d(pT)4 and d(pT)10. Since the Ids of 2C3 Ig express germ-line encoded Vk1 gene, it was of interest to determine if this anti-DNA response is down-regulated in non-autoimmune BALB/c mice. To assess this, six synthetic peptides based on the amino acid sequences of the Ids of 2C3 and four peptides corresponding to the Ids of non-Vk 1 related anti-DNA Ab were chosen to stimulate splenic T-cells from naive BALB/c and (NZBxW F1) mice. Among these peptides, VL1 encompassing **complementarity-determining region 1** of 2C3 light chain induces specific CD8+ CTLs in normal BALB/c mice. VL1-peptide does not induce CTL in (NZBxW) F1 mice. CTLs from VL1-stimulated T-cells are cytotoxic to 2C3 hybridoma and VL1-peptide pulsed P815 cells, and inhibited by antibodies specific for MHC class I, beta2 microglobulin, and CD8 molecules. VL1 (Id)-specific CTLs are induced in BALB/c mice as a mechanism to counter induction of auto-reactive anti-DNA B-cells.

LS ANSWER 3 OF 15 MEDLINE
 AN 2002055642 MEDLINE
 DN 21640007 PubMed ID: 11781155
 TI Systemic lupus erythematosus patients under immunosuppressive treatment express high levels of the immunoglobulin lambda variable IGLV8S1 gene with silent somatic mutations.
 AU Tamia-Perreira Marcia Cristina; Trevisan Glaucio L; de Carvalho Ivan Fiore; Passos Geraldo A S
 CS Grupo de Imunogenetica Molecular, Departamento de Genetica, Faculdade de Medicina de Ribeirao Preto, Universidade de Sao Paulo, Brazil.
 SO BIOCHIMICA ET BIOPHYSICA ACTA, (2002 Jan 2) 1586 (1) 108-12.
 CY Netherlands
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 OS GENBANK-AF411519; GENBANK-AF411520; GENBANK-AF411521; GENBANK-AF411522; GENBANK-AF411523
 EM 200203
 ED Entered STN: 20020125
 Last Updated on STN: 20020308
 Entered Medline: 20020307
 AB Systemic lupus erythematosus (SLE) patients express high titers of somatically mutated serum autoantibodies against nuclear structures including double-stranded DNA. These somatic mutations accumulate codons for basic amino acids in the immunoglobulin variable regions of both, heavy and light chains, facilitating **binding to nucleic acids**. The variable (V) immunoglobulin lambda 8 (IGLV8S1) gene contributes to autoreactive B-cell repertoire of auto-immune patients. Accumulation of immune complexes of these anti-DNA autoantibodies causes severe systemic inflammation in SLE. The current treatment of lupus disease is based on immunosuppressive drugs, but the precise role for this therapy remains to be defined. To evaluate the in vivo effect of combined immunosuppressive treatment on B-lymphocytes repertoire of SLE patients, we have developed an approach using the IGLV8S1 gene as a marker. The transcription of this gene in treated SLE patients was increased. However, we observed a trend, in these patients, to conserve **complementarity determining regions** (CDRs) and framework regions (FRs) of VLambda8 polypeptide light chain deduced sequence, from its germline counterpart. Sequencing IGLV8S1 cDNA of untreated SLE patients, taken as a control for treatment effect, displayed a decreased frequency of silent somatic mutations (consequently high

frequency of replacement mutations) in the V λ mbda8 polypeptide chain deduced sequence. These data suggest that the immunosuppressive drug treatment modulates the positive selection of somatically mutated V λ mbda8 light chain.

LS ANSWER 4 OF 15 MEDLINE DUPLICATE 3
AN 2001250834 MEDLINE
DN 21244632 PubMed ID: 11320219
TI Protein quantification from complex protein mixtures using a proteomics methodology with single-cell resolution.
AU Zhang H T; Kacharmina J E; Miyashiro K; Greene M I; Eberwine J
CS Department of Pathology, Abramson Institute for Cancer Research, University of Pennsylvania, Philadelphia, PA 19104-6082, USA.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2001 May 8) 98 (10) 5497-502.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200106
ED Entered STN: 20010618
Last Updated on STN: 20030105
Entered Medline: 20010614
AB We have developed an extremely sensitive technique, termed immuno-detection amplified by T7 RNA polymerase (IDAT) that is capable of monitoring proteins, lipids, and metabolites and their modifications at the single-cell level. A double-stranded oligonucleotide containing the T7 promoter is conjugated to an antibody (Ab), and then T7 RNA polymerase is used to amplify RNA from the double-stranded **oligonucleotides coupled** to the Ab in the Ab-antigen complex. By using this technique, we are able to detect the p185 (her2/neu) receptor from the crude lysate of T6-17 cells at 10(-13) dilution, which is 10(9)-fold more sensitive than the conventional ELISA method. Single-chain Fv fragments or **complementarity determining region** peptides of the Ab also can be substituted for the Ab in IDAT. In a modified protocol, the **oligonucleotide** has been **coupled** to an Ab against a common epitope to create a universal detector species. With the linear amplification ability of T7 RNA polymerase, IDAT represents a significant improvement over immuno-PCR in terms of sensitivity and has the potential to provide a robotic platform for proteomics.

LS ANSWER 5 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
AN 2000:33233 BIOSIS
DN PREV200000033233
TI Thermodynamics of Fab-ssDNA interactions: Contribution of heavy chain complementarity determining region 3.
AU Komissarov, Andrey A.; Deutscher, Susan L. (1)
CS (1) Department of Biochemistry, University of Missouri School of Medicine, M121 Medical Sciences Building, Columbia, MO, 65212 USA
SO Biochemistry, (Nov. 2, 1999) Vol. 38, No. 44, pp. 14631-14637.
ISSN: 0006-2960.
DT Article
LA English
SL English
AB The recombinant anti-ssDNA Fab, DNA-1, and 16 heavy chain **complementarity determining region 3** (HCDR3) mutant variants were selected for thermodynamic characterization of ssDNA binding. The affinity of Fab to (dT)15 under different temperatures and cation concentrations was measured by equilibrium fluorescence quenching titration. Changes in the standard Gibbs free binding energy (DELTA Gdegree), enthalpy (DELTA Hdegree), entropy (DELTA Sdegree), and the

number of ionic pairs (Z) formed upon interaction were determined. All Fab possessed an enthalpic nature of interaction with ssDNA, that was opposite to the previously reported entropically driven binding to dsDNA (Tanha, J., and Lee, J. S. (1997) *Nucleic Acids Res.* 25, 1442-1449). The contribution of separate residues of HCDR3 to ssDNA interaction was investigated. Analysis of the changes in DELTAHdegree and TDELTAHdegree, induced by substitutions in HCDR3, revealed a complete entropy/enthalpy compensation. Mutations R98A and D108A at the ends of the HCDR3 loop produced increases in TDELTAHdegree by 10.4 and 15.9 kcal/mol, respectively. Substitution of proline for arginine at the top of HCDR3 resulted in a new electrostatic contact with (dT)15. The observed linear correlation of Z and DELTAHdegree of nonelectrostatic interactions (DELTAHdegreegreenonell) at the anti-ssDNA combining site was used for the estimation of the specific DELTAHdegreegreenonell (-20 to -25 cal/(molcndotANG2)), the average contact area (450-550 ANG2), the maximal Z (6-7), and the limit in affinity under standard cation concentrations ((0.5-1) X 108 M-1) for this family of Fab. Results suggested that rational engineering of HCDR3 could be utilized to control the affinity and likely the specificity of Ab-DNA interactions.

L5 ANSWER 6 OF 15 MEDLINE DUPLICATE 5
 AN 2000016379 MEDLINE
 DN 20016379 PubMed ID: 10547287
 TI Fabs specific for 8-oxoguanine: control of DNA binding.
 AU Bespalov I A; Bond J P; Purmal A A; Wallace S S; Melamed R J
 CS Department of Microbiology and Molecular Genetics, The Markey Center for Molecular Genetics, University of Vermont, Burlington, VT 05405, USA.
 SO JOURNAL OF MOLECULAR BIOLOGY, (1999 Nov 12) 293 (5) 1085-95.
 Journal code: 2985088R. ISSN: 0022-2836.
 CY ENGLAND: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 OS GENBANK-AF104995; GENBANK-AF104996; GENBANK-AF104997; GENBANK-AF104998; GENBANK-AF104999; GENBANK-AF105000; GENBANK-AF105001
 EM 200001
 ED Entered STN: 20000124
 Last Updated on STN: 20000124
 Entered Medline: 20000111
 AB Free radicals produce a broad spectrum of DNA base modifications including 7,8-dihydro-8-oxoguanine (8-oxoG). Since free radicals have been implicated in many pathologies and in aging, 8-oxoG has become a benchmark for factors that influence free radical production. Fab g37 is a monoclonal antibody that was isolated by phage display in an effort to create a reagent for detecting 8-oxoG in DNA. Although this antibody exhibited a high degree of specificity for the 8-oxoG base, it did not appear to recognize 8-oxoG when present in DNA. Fab g37 was modified using HCDR1 and HCDR2 segment shuffling and light chain shuffling. Fab 166 and Fab 366 which bound to 8-oxoG in single-stranded DNA were isolated. Fab 166 binds more selectively to single-stranded oligonucleotides containing 8-oxoG versus control oligonucleotides than does Fab 366 which binds DNA with reduced dependency on 8-oxoG. Numerous other clones were also isolated and characterized that contained a spectrum of specificities for 8-oxoG and for DNA. Analysis of the primary sequences of these clones and comparison with their binding properties suggested the importance of different complementarity determining regions and residues in determining the observed binding phenotypes. Subsequent chain shuffling experiments demonstrated that mutation of SerH53 to ArgH53 in the Fab g37 heavy chain slightly decreased the Fab's affinity for 8-oxoG but significantly improved its binding to DNA in an 8-oxoG-dependent manner. The light chain shuffling experiments also demonstrated that numerous promiscuous light chains could enhance DNA binding when paired with either the Fab g37 or Fab 166 heavy chains;

however, only the Fab 166 light chain did so in an additive manner when combined with the Fab 166 heavy chain that contains ArgH53. A three-point model for Fab 166 **binding to oligonucleotides** containing 8-oxoG is proposed. We describe a successful attempt to generate a desired antibody specificity, which was not present in the animal's original immune response.
Copyright 1999 Academic Press.

L5 ANSWER 7 OF 15 MEDLINE DUPLICATE 6
AN 1999036654 MEDLINE
DN 99036654 PubMed ID: 9819225
TI Isolation and characterization of a monoclonal anti-quadruplex DNA antibody from autoimmune "viable motheaten" mice.
AU Brown B A 2nd; Li Y; Brown J C; Hardin C C; Roberts J F; Pelsue S C; Shultz L D
CS Department of Biochemistry, North Carolina State University, Raleigh 27695, USA.
NC CA20408 (NCI)
DK07449 (NIDDK)
GM47431 (NIGMS)
SO BIOCHEMISTRY, (1998 Nov 17) 37 (46) 16325-37.
Journal code: 0370623. ISSN: 0006-2960.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199812
ED Entered STN: 19990115
Last Updated on STN: 20000303
Entered Medline: 19981217
AB A cell line that produces an autoantibody specific for DNA quadruplex structures has been isolated and cloned from a hybridoma library derived from 3-month-old nonimmunized autoimmune, immunodeficient "viable motheaten" mice. This antibody has been tested extensively in vitro and found to bind specifically to DNA quadruplex structures formed by two biologically relevant sequence motifs. Scatchard and nonlinear regression analyses using both one- and two-site models were used to derive association constants for the antibody-DNA binding reactions. In both cases, quadruplexes had higher association constants than triplex and duplex molecules. The anti-quadruplex antibody **binds** to the quadruplex formed by the promoter-region-derived **oligonucleotide** d(CGCG4GCG) ($K_a = 3.3 \times 10(6) \text{ M}^{-1}$), and has enhanced affinity for telomere-derived quadruplexes formed by the oligonucleotides d(TG4) and d(T2G4T2G4T2G4T2G4) ($K_a = 5.38 \times 10(6)$ and $1.66 \times 10(7) \text{ M}^{-1}$, respectively). The antibody binds both types of quadruplexes but has preferential affinity for the parallel four-stranded structure. In vitro radioimmunoassay binding experiments demonstrated that purified anti-DNA quadruplex antibodies from anti-quadruplex antibody-producing tissue culture supernatants have at least 10-fold higher affinity for quadruplexes than for triplex and duplex DNA structures of similar base composition and length. The antibody binds intramolecular DNA triplexes formed by d(G4T3G4T3C4) and d(C4T3G4T3G4), and the duplex d(CGCGCGCGCG)2 with affinities of $6.76 \times 10(5)$, $5.59 \times 10(5)$, and $8.26 \times 10(5) \text{ M}^{-1}$, respectively. Competition experiments showed that melted quadruplexes are not effective competitors for antibody binding when compared to native structures, confirming that the quadruplex is bound structure-specifically. To our knowledge, this is the first immunological reagent known to specifically recognize quadruplex structures. Subsequent sequence analysis demonstrates homologies between the antibody **complementarity determining regions** and sequences from Myb family telomere binding proteins, which are hypothesized to control cell aging via telomeric DNA interactions. The presence of this antibody in the autoimmune repertoire suggests a possible linkage between autoimmunity, telomeric DNA binding proteins, and aging.

L5 ANSWER 8 OF 15 MEDLINE DUPLICATE 7
 AN 1999065330 MEDLINE
 DN 99065330 PubMed ID: 9850078
 TI Immunity to p53 induced by an idiotypic network of anti-p53 antibodies: generation of sequence-specific anti-DNA antibodies and protection from tumor metastasis.
 AU Erez-Alon N; Herkel J; Wolkowicz R; Ruiz P J; Waisman A; Rotter V; Cohen I R
 CS Department of Immunology, Weizmann Institute of Science, Rehovot, Israel.
 SO CANCER RESEARCH, (1998 Dec 1) 58 (23) 5447-52.
 Journal code: 2984705R. ISSN: 0008-5472.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199812
 ED Entered STN: 19990115
 Last Updated on STN: 19990115
 Entered Medline: 19981231
 AB The general overexpression of p53 by different types of tumor cells suggests that p53 immunity might be generally useful for tumor immunotherapy. We describe here the induction of immunity to p53 and resistance to tumor metastasis using an idiotypic network. Mice were immunized with domain-specific anti-p53 monoclonal antibodies (Ab1): PAB-248 directed to the N-terminus; PAB-246 directed to the specific DNA-binding region; or PAB-240 directed to a mutant p53 that does not bind specific DNA. Immunized mice responded by making anti-idiotypic antibodies (Ab2) specific for the Ab1 inducer. Ab1 PAB-246 induced Ab2 that, like p53 itself, could bind the specific DNA oligonucleotide sequence of the p53 responsive element. Mice immunized with Ab1 PAB-240 or PAB-246 spontaneously made Ab3 anti-p53 antibodies that reflected the specificity of their Ab1 inducers: Ab1 PAB-246 induced Ab3 specific for wild-type p53; PAB-240 induced Ab3 specific for mutant p53. Ab1 PAB-248 induced only Ab2. The spontaneously arising Ab3 were of T cell-dependent IgG isotypes. Peptides from the complementarity determining regions of the Ab1 antibodies PAB-240 and PAB-246 could also induce Ab3 anti-p53. Finally, mice that produced Ab3 anti-p53 acquired resistance to tumor metastases. Therefore, an anti-idiotypic network built around certain domains of p53 seems to be programmed within the immune system, specific Ab2 antibodies can mimic the DNA binding domain of p53, and Ab3 network immunity to p53 can be associated with resistance to tumor cells.

L5 ANSWER 9 OF 15 MEDLINE DUPLICATE 8
 AN 96218138 MEDLINE
 DN 96218138 PubMed ID: 8647821
 TI Equilibrium binding studies of recombinant anti-single-stranded DNA Pab. Role of heavy chain complementarity-determining regions.
 AU Komissarov A A; Calcutt M J; Marchbank M T; Peletskaya E N; Deutscher S L
 CS Department of Biochemistry, University of Missouri School of Medicine, Columbia 65212, USA.
 NC GM-47979 (NIGMS)
 SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 May 24) 271 (21) 12241-6.
 Journal code: 2985121R. ISSN: 0021-9258.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199607
 ED Entered STN: 19960805
 Last Updated on STN: 19960805
 Entered Medline: 19960722
 AB We previously isolated nucleic acid-binding

antibody fragments (Fab) from bacteriophage display libraries representing the immunoglobulin repertoire of autoimmune mice to expedite the analysis of antibody-DNA recognition. In the present study, the binding properties of one such anti-DNA Fab, high affinity single-stranded (ss) DNA-binding Fab (DNA-1), were defined using equilibrium gel filtration and fluorescence titration. Results demonstrated that DNA-1 had a marked preference for oligo(dT) (100 nM dissociation constant) and required oligo(dT) >5 nucleotides in length. A detailed analysis of the involvement of the individual heavy chain (H) **complementarity-determining regions** (CDR) ensued using previously constructed HCDR transplantation mutants between DNA-1 and low affinity ssDNA-binding Fab (D5), a Fab that binds poorly to DNA (Calcutt, M. J. Komissarov, A. A., Marchbank, M. T., and Deutscher, S. L. (1996) *Gene* (Amst.) 168, 9-14). Circular dichroism studies indicated that the wild type and mutant Fab studied were of similar overall secondary structure and may contain similar combining site shapes. The conversion of D5 to a high affinity oligo(dT)-binding Fab occurred only in the presence of DNA-1 HCDR3. Results with site-specific mutants in HCDR1 further suggested a role of residue 33 in interaction with nucleic acid. The results of these studies are compared with previously published data on DNA-antibody recognition.

L5 ANSWER 10 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 9

AN 1996:156003 BIOSIS

DN PREV199698728138

TI Recombinant phabs reactive with 7,8-dihydro-8-oxoguanine, a major oxidative DNA lesion.

AU Bepalov Vvan A., Andrei A. Purmal; Glackin, Mary P.; Wallace, Susan S. (1); Melamede, Robert J.

CS (1) Dep. Microbiol. Mol. Genet., Markey Cent. Mol. Genet., Univ. Vermont, Stafford Hall, Burlington, VT 05405 USA

SO Biochemistry, (1996) Vol. 35, No. 7, pp. 2067-2078. ISSN: 0006-2960.

DT Article

LA English

AB Antibody Fabs that bind to DNA damages provide useful models for understanding DNA damage-specific protein interactions. BSA and RSA conjugates of the nucleoside and nucleotide derivatives of the oxidative DNA lesions, 7,8-dihydro-8-oxoguanine (8-oxoG) and 7,8-dihydro-8-oxoadenine (8-oxoA), were used to immunize mice. RNA from the responders was isolated and used to repertoire clone and phage display Fabs that bind to these haptens. Direct binding and competitive enzyme-linked immunosorbent assay (ELISA) demonstrated that phage Fabs (Phabs) specific for 8-oxopurine-BSA conjugates and 8-oxoguanine were produced although the Phabs did not react with 8-oxopurines in DNA. Amino acid sequence comparisons among clones having different binding properties suggested that a relatively small portion of the binding surfaces defined by the **complementarity determining regions** (CDR) accounted for hapten binding specificity, whereas other regions appeared to stabilize hapten binding by interacting with protein or DNA epitopes. Chain shuffling between 8-oxopurine-BSA binding Fabs and a DNA binding Fab showed that the heavy chain of the DNA binder conferred DNA binding capacity to the light chain of only one of the 8-oxopurine-BSA binders. Homology modeling of the 8-oxoG-specific clone g37 showed significant similarities to two previously isolated monoclonal antibodies specific for single-stranded **nucleic acids**. In the 8-oxoG Fab, which did not bind to DNA, the presumptive DNA binding canyon was blocked by heavy chain residues in the CDR2 region and appeared to lack part of the canyon wall due to the different placement of the light chain framework region.

L5 ANSWER 11 OF 15 MEDLINE

AN 96186948 MEDLINE

DUPLICATE 10

DN 96186948 PubMed ID: 8626072
 TI Analysis of a **nucleic-acid-binding** antibody
 fragment: Construction and characterization of heavy-chain
complementarity-determining region switch
 variants.
 AU Calcutt M J; Komissarov A A; Marchbank M T; Deutscher S L
 CS Department of Molecular Microbiology and Immunology, University of
 Missouri, Columbia, 65212, USA.
 NC SR29 GM47979 (NIGMS)
 SO GENE, (1996 Feb 2) 168 (1) 9-14.
 Journal code: 7706761. ISSN: 0378-1119.
 CY Netherlands
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199606
 ED Entered STN: 19960708
 Last Updated on STN: 19960708
 Entered Medline: 19960621

AB The display of antibody (AB) fragments (Fab) on the surface of filamentous
 bacteriophage (phage) and selection of phage that interact with a
 particular antigen (Ag) has enabled the isolation of Fab that bind
nucleic acids. Nucleic acid (NA)
binding Ab occur in vivo in connective tissue disease patients and
 certain inbred strains of mice and are thought to be pathogenic. Although
 there is ample data concerning the amino acid (aa) sequence of murine
 monoclonal Ab (mAb) reactive with DNA, significantly less is known about
 how autoAb interact with NA. The **complementarity-**
determining regions (CDR) contained in the Fab
 contribute to most Ag binding, especially through heavy (H)-chain CDR 3.
 We have examined the role of individual H-chain CDR of a previously
 isolated recombinant single-stranded DNA-binding Fab (DNA-1) in
nucleic acid interaction using a combination of H-chain
 CDR switching and solution-binding experiments. The three H-chain CDR of
 DNA-1 Fab were independently switched with the H-chain CDR of a Fab (D5)
 with very similar sequence and framework (FR) that binds DNA poorly in
 order to create all possible H-chain CDR combinations. The chimeric Fab
 genes were bacterially expressed, and their products were purified and
 analyzed. Results indicated that the H-chain CDR 3 of DNA-1 Fab, in the
 context of the remainder of the H-chain of D5 Fab, restored binding to
 oligo(dT)15 to 60% of DNA-1 levels, whereas H-chain CDR 1 and 3 of DNA-1
 with CDR 2 of D5 Fab restored binding to 100% A combination of H-chain CDR
 2 and 3 of DNA-1 Fab with H-chain CDR 1 of D5, unexpectedly resulted in
 the ability of the chimeric Fab to bind RNA preferentially over DNA.
 These studies demonstrate the importance of both H-chain CDR 1 and 3 in
 DNA recognition and further suggest that the specificity of the type of NA
 recognized by a particular Fab can be drastically altered by exchanging
 CDR.

L5 ANSWER 12 OF 15 MEDLINE
 AN 95223974 MEDLINE
 DN 95223974 PubMed ID: 7708679
 TI Human autoantibody recognition of DNA.
 AU Barbas S M; Ditzel H J; Salonen E M; Yang W P; Silverman G J; Burton D R
 CS Department of Immunology, Scripps Research Institute, La Jolla, CA 92037,
 USA.
 SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF
 AMERICA, (1995 Mar 28) 92 (7) 2529-33.
 Journal code: 7505876. ISSN: 0027-8424.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals; AIDS
 EM 199505

DUPLICATE 11

ED Entered STN: 19950518
Last Updated on STN: 19970203
Entered Medline: 19950511

AB Combinatorial IgG Fab phage display libraries prepared from a systemic lupus erythematosus (SLE) donor and a healthy donor were affinity selected against human placental DNA. Human monoclonal antibody Fab fragments specific for DNA were isolated from both libraries, although Fabs of the highest affinity were isolated only from the lupus library. Generally, apparent affinities of the Fabs for human placental DNA, purified double-stranded DNA, and denatured DNA were approximately equivalent. Surface plasmon resonance indicated Fab binding constants for a double-stranded oligodeoxynucleotide of $0.2-1.3 \times 10^8$ M⁻¹. The higher-affinity Fabs, as ranked by binding to human placental DNA or to the oligonucleotide probe, tested positive in the Crithidia lucilliae assay commonly used in the diagnosis of SLE, and interestingly the genes encoding the heavy-chain variable regions of these antibodies displayed evidence of only minimal somatic hypermutation. The heavy chains of the SLE Fabs were characterized by a predominance of basic residues toward the N terminus of **complementarity-determining region 3 (CDR3)**. The crucial role of heavy-chain CDR3 (HCDR3) in high-affinity DNA recognition was suggested by the creation of DNA binding in an unrelated antibody by HCDR3 transplantation from SLE antibodies. We propose that high-affinity DNA-binding antibodies can arise in SLE without extensive somatic hypermutation in the variable-region genes because of the expression of inappropriate HCDR3s.

L5 ANSWER 13 OF 15 MEDLINE DUPLICATE 12
AN 94148867 MEDLINE
DN 94148867 PubMed ID: 8106407
TI Sequencing and modeling of anti-DNA immunoglobulin Fv domains. Comparison with crystal structures.
AU Barry M M; Mol C D; Anderson W F; Lee J S
CS Department of Biochemistry, University of Saskatchewan, Saskatoon, Canada.
NC DK42502 (NIDDK)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Feb 4) 269 (5) 3623-32.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199403
ED Entered STN: 19940330
Last Updated on STN: 19940330
Entered Medline: 19940318

AB Models for the three-dimensional structures of the combining regions of six DNA-binding antibodies have been derived from the sequence data for their Fv domains presented here. Using the amino acid sequences and the canonical structure classes described by Chothia and Lesk (Chothia, C., and Lesk, A.M. (1987) J. Mol. Biol. 196, 901), model loops were selected from immunoglobulin domains of known structure for five of the six antibody hypervariable regions. Models for the third **complementarity-determining region** of the heavy chain were constructed from known immunoglobulin loops of similar length and sequence. Comparison of three of the models with the respective crystal structure indicates that this procedure can generate a working model of the antibody combining region that provides useful information on the nature of the interactions between antibodies and nucleic acids. As part of our continuing investigation into the structural basis of antibody-DNA recognition, the observed and predicted models for the combining regions of **nucleic acid-binding** antibodies have been examined. In general, single strand-specific antibodies have deep clefts where the antigen might bind, whereas duplex-specific antibodies present a relatively flat surface. In

addition, on the basis of both sequence and structure, there is little to distinguish autoimmune antibodies from those produced by immunization. Testable hypotheses for how these antibodies might interact with single- and double-stranded nucleic acids are presented.

- L5 ANSWER 14 OF 15 MEDLINE DUPLICATE 13
 AN 94280777 MEDLINE
 DN 94280777 PubMed ID: 8011289
 TI Genetic and structural evidence for antigen selection of anti-DNA antibodies.
 AU Radic M Z; Weigert M
 CS Department of Microbiology and Immunology, Medical College of Pennsylvania, Philadelphia 19129.
 NC CA-06927 (NCI)
 GM-20964 (NIGMS)
 RR-05539 (NCRR)
 SO ANNUAL REVIEW OF IMMUNOLOGY, (1994) 12 487-520. Ref: 90
 Journal code: 8309206. ISSN: 0732-0582.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, ACADEMIC)
 LA English
 FS Priority Journals
 EM 199407
 ED Entered STN: 19940810
 Last Updated on STN: 19940810
 Entered Medline: 19940727
- AB The primary structure of anti-DNA antibodies is highly diverse, a result of different germline variable (V) gene use, different combinations of immunoglobulin gene segments, peculiar heavy chain **complementarity determining region 3** (H-CDR3) segments, and somatic mutations. Nevertheless, tertiary structure predictions reveal common features that yield information about likely contact sites in the anti-DNA combining site. That these contacts are involved with DNA binding is supported by recurrent features of a newly compiled set of homology groups of 13 variable regions of heavy chains (VH) and 11 variable regions of light chains (VL), characteristic pattern of somatic mutations, and the results of site-directed mutagenesis. The role of antigen in the etiology of the autoimmune response is viewed in light of recent data on overlaps between anti-DNA and anti-nucleic acid binding protein specificities.
- L5 ANSWER 15 OF 15 MEDLINE DUPLICATE 14
 AN 95085854 MEDLINE
 DN 95085854 PubMed ID: 7993703
 TI Autoantibodies in systemic lupus erythematosus.
 AU Rahman M A; Isenberg D A
 CS University College, London, United Kingdom.
 SO CURRENT OPINION IN RHEUMATOLOGY, (1994 Sep) 6 (5) 468-73. Ref: 47
 Journal code: 9000851. ISSN: 1040-8711.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
 LA English
 FS Priority Journals
 EM 199501
 ED Entered STN: 19950126
 Last Updated on STN: 19950126
 Entered Medline: 19950119
- AB Various autoantibodies are found in systemic lupus erythematosus. Anti-double-stranded DNA antibodies are the most pathognomonic and among the most extensively studied. Genetic studies of these antibodies and

their idiotypes suggest that high-affinity IgG anti-double-stranded DNA antibodies are produced by a process of somatic mutation and clonal expansion favoring sequences with accumulated positively charged amino acids in the **complementarity-determining regions**. The antigens that trigger this process are not known, but recent studies have suggested that a DNA-protein complex may be implicated. At the tissue level, these antibodies may react directly with membrane proteins or indirectly via complexes with DNA, histones, and heparan sulfate. Serologic studies have sought to establish links between clinical features and the presence of particular non-DNA-binding autoantibodies. Of particular interest have been antibodies to proteins with **nucleic acid-binding** potential, such as Sm, SS-A (Ro), and SS-B (La).

=> s l1 and kit#

L6 0 L1 AND KIT#

=>

09624.946

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<u>L4</u>	L3 and (epitope\$1 or antibod\$3 or antigen\$1)	17	<u>L4</u>
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<u>L3</u>	L2 and kit\$1	18	<u>L3</u>
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<u>L2</u>	Fv near10 (coupl\$3 or attach\$3 or bind\$3) near10 (nucleic acid\$1 or oligonucleotide\$1)	28	<u>L2</u>
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DB=DWPI,USPT,EPAB,JPAB; PLUR=YES; OP=ADJ

<u>L1</u>	single chain Fv near5 (coupl\$3 or attach\$3 or bind\$3) near5 (oligonucleotide\$1 or nucleic acid\$1)	2	<u>L1</u>
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END OF SEARCH HISTORY

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Search Results - Record(s) 11 through 17 of 17 returned.

☐ 11. 5877305. 12 Dec 94; 02 Mar 99. DNA encoding biosynthetic binding protein for cancer marker. Huston; James S., et al. 536/23.53; 424/133.1 435/328 435/69.6 530/387.3. A61K039/395.

☐ 12. 5807826. 08 Apr 97; 15 Sep 98. Semaphorin gene family. Goodman; Corey S., et al. 514/12; 514/14 514/15 514/16 514/17 514/21. A61K038/04 A61K038/16.

☐ 13. 5723287. 03 May 95; 03 Mar 98. Recombinant viruses displaying a nonviral polypeptide on their external surface. Russell; Stephen J., et al. 435/5; 435/235.1 435/6 536/23.4 536/23.72. C12Q001/70 C12Q001/68 C12N001/00 C07H021/04.

☐ 14. 5639856. 13 Sep 93; 17 Jun 97. Semaphorin gene family. Goodman; Corey S., et al. 530/326; 530/327 530/328 530/329 530/330 530/350. A61K038/04 A61K038/16 C07K014/005 C07K014/435.

☐ 15. 5565331. 12 Nov 93; 15 Oct 96. Nucleic acids encoding neural axon outgrowth modulators. Tessier-Lavigne; Marc, et al. 435/69.1; 435/320.1 435/6 536/23.5. C12N015/00 C12N015/12 C12N005/10.

☐ 16. US 20020094534 A1 WO 200266980 A1. Detecting molecules expressing epitope, by contacting surface immobilized molecule with epitope detector, amplifying and contacting oligonucleotide bound to molecule with fluorescent dye, measuring emitted fluorescence. GREENE, M I, et al. C07H021/02 C07H021/04 C12N001/20 C12P019/34 C12Q001/68 G01N033/48 G01N033/53.

☐ 17. US 20020028450 A1. Detecting molecules expressing a selected epitope in a sample involves using epitope detector containing single chain Fv for the selected epitope or a constrained epitope specific CDR attached to an oligonucleotide. GREENE, M I, et al. C12P019/34 C12Q001/68.

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